

# BCCA Protocol Summary for Primary Treatment of No Visible Residual (Moderate-High Risk) Invasive Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer Using **CARBO**platin and **PACLI**taxel

**Protocol Code:** GOOVCATM

**Tumour Group:** Gynecology

**Contact Physicians:** Dr. Ken Swenerton

## ELIGIBILITY:

- invasive epithelial ovarian, fallopian tube and primary peritoneal cancer, with no visible residual tumour, or borderline with invasive implants
- FIGO Ia: Grade 2 or 3
- FIGO Ib: Grade 2 or 3
- FIGO Ic, II, or III: any Grade

## EXCLUSIONS:

- visible residual tumour (use GOOVCATX or GOOVCADX)
- AST and/or ALT greater than 10 times the Upper Limit of Normal (ULN)
- total bilirubin greater than 128 micromol/L

## RELATIVE CONTRAINDICATIONS:

- pre-existing motor or sensory neuropathy greater than grade 2
- performance status greater than ECOG 3

## TESTS:

- Baseline: CBC & diff, platelets, creatinine, tumour marker (CA 125, CA 15-3, CA 19-9), LFT's (if abnormal liver function is a potential concern), camera nuclear renogram for GFR (optional)
- Day 14 (and Day 21 if using 4 week interval) of first cycle (and in subsequent cycle(s) if a dose modification has been made): CBC & diff, platelets. No need for interim count check once safe nadir pattern has been established.
- Before each treatment: CBC & diff, any initially elevated tumour marker, LFT's (if clinically indicated), creatinine (if clinically indicated e.g., third space fluid, marked emesis, poor oral intake).

## PREMEDICATIONS:

- **PACLI**taxel must not be started unless the following drugs have been given:
  - 45 minutes prior to **PACLI**taxel:
    - Dexamethasone 20 mg IV in 50 mL NS over 15 minutes
  - 30 minutes prior to **PACLI**taxel:
    - Diphenhydramine 50 mg IV and Ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)
- Ondansetron 8 mg po 30 minutes pre-**CARBO**platin

## ANTIEMETIC THERAPY POST-CHEMOTHERAPY:

- Antiemetic protocol for moderate emetogenic chemotherapy protocols (see SCNAUSEA)
- Dexamethasone 4 mg PO BID for 2 days and Dimenhydrinate 50-100 mg PRN after treatment is usually adequate

**SYSTEMIC TREATMENT** (give **PACLI**taxel first):

Drug	Starting Dose	BCCA Administration Standard
<b>PACLI</b> taxel	175 mg/m <sup>2</sup> *	IV in 500 mL NS over 3 hours (use non-PVC equipment, in-line filter)
<b>CARBO</b> platin	Dose = AUC** x (GFR +25)	IV in 250 mL D5W over 30 minutes

\* Conservative dosing (i.e., 155 mg/m<sup>2</sup> or 135 mg/m<sup>2</sup>) may be considered in the following cases: ECOG greater than 2, existing or potential myelosuppression; existing or potential arthralgia and myalgia; prior radiotherapy, particularly to the pelvic region; reduced bone marrow capacity. An initial dose of 135 mg/m<sup>2</sup> is recommended in patients greater than 75 years of age, with escalation to 155 mg/m<sup>2</sup> and then 175 mg/m<sup>2</sup> if tolerated.

\*\* use AUC of 6; if extensive prior radiation therapy, use AUC of 5

Repeat every 21-28 days for: (a) 3 cycles, if to be followed by radiation therapy; or  
(b) 6 cycles, if radiation therapy is not planned (papillary serous histology or contraindication to use of irradiation)

*Measured GFR* (e.g. nuclear renogram) is preferred in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, age greater than 70, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; [the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence.](#)

**Cockcroft-Gault Formula**

$$\text{GFR} = \frac{1.04 \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

Recalculate GFR if, at a point of (optional) checking, creatinine increases by greater than 20% or rises above the upper limit of normal.

**DOSE MODIFICATIONS:**

1. **Hematology:**

a) on treatment day:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	Doses (both drugs)
greater than or equal to 1	and	greater than or equal to 100	treat as per nadir (if applicable); otherwise, proceed at same doses
less than 1	or	less than 100	Delay until recovery. If using 21-day interval, switch to 28-day interval. If 2 <sup>nd</sup> delay, use G-CSF or dose reduction.

\* If ANC greater than 0.8 and monocytes greater than or equal to 20%, neutrophil count recovery is likely imminent. Continuation without delay may occur at physician's discretion.

b) at nadir (until nadir pattern established):

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	PACLItaxel	CARBOplatin*
greater than or equal to 1.5	and	greater than or equal to 100	100%	120%**
0.5-1.4	and	greater than or equal to 75	100%	100%
less than 0.5	and	less than 75	80%	80%
less than 0.5	and	greater than or equal to 75	80%	100%
greater than or equal to 0.5	and	less than 75	100%	80%
febrile neutropenia at any time			80%	80%

\* % of previous cycle's dose, at physician's discretion. If dose is changed, subsequent nadir counts must be checked.

\*\* If dose has been reduced, dose increase/re-escalation for good nadir counts is not recommended.

- Arthralgia and/or myalgia:** If arthralgia and/or myalgia of grade 2 (moderate) or higher was not adequately relieved by NSAIDs or acetaminophen with codeine (e.g., TYLENOL #3®), a limited number of studies report a possible therapeutic benefit using:
  - Prednisone 10 mg PO bid x 5 days starting 24 hours post-PACLItaxel
  - Gabapentin 300 mg PO on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 5-15 days (based on duration of arthromyalgia)
 If arthralgia and/or myalgia persists, reduce subsequent PACLItaxel doses to 135 mg/m<sup>2</sup> or switch taxane to DOCEtaxel (GOOVCADM)
- Neuropathy:** Dose modification or discontinuation may be required (see BCCA Cancer Drug Manual).
- Renal dysfunction:** If significant increase (greater than 20% or rises above the upper limit of normal) in creatinine, recheck/recalculate GFR and recalculate CARBOplatin dose using new GFR.
- Hepatic dysfunction:** Dose reduction may be required for PACLItaxel.

ALT		Bilirubin	Dose
less than 10 x ULN	and	less than or equal to 1.25 x ULN	175 mg/m <sup>2</sup>
less than 10 x ULN	and	1.26-2 x ULN	135 mg/m <sup>2</sup>
less than 10 x ULN	and	2.01-5 x ULN	90 mg/m <sup>2</sup>
greater than or equal to 10 x ULN	and/or	greater than 5 x ULN	not recommended

**PRECAUTIONS:**

1. **Hypersensitivity:** Reactions to **PACLI**taxel are common. See BCCA Hypersensitivity Guidelines

<i>Mild</i> symptoms (e.g. mild flushing, rash, pruritus)	<ul style="list-style-type: none"><li>▪ complete <b>PACLI</b>taxel infusion. Supervise at bedside</li><li>▪ no treatment required</li></ul>
<i>moderate</i> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"><li>▪ stop <b>PACLI</b>taxel infusion</li><li>▪ give IV DiphenhydrAMINE 25-50 mg and Hydrocortisone IV 100 mg</li><li>▪ after recovery of symptoms resume <b>PACLI</b>taxel infusion at 20 mL/h for 5 minutes, 30 mL/h for 5 minutes, 40 mL/h for 5 minutes, then 60 mL/h for 5 minutes. If no reaction, increase to full rate.</li><li>▪ if reaction recurs, discontinue <b>PACLI</b>taxel therapy</li></ul>
<i>severe</i> symptoms (i.e. <i>one</i> or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"><li>▪ stop <b>PACLI</b>taxel infusion</li><li>▪ give IV antihistamine and steroid as above. Add Epinephrine or bronchodilators if indicated</li><li>▪ discontinue <b>PACLI</b>taxel therapy</li></ul>

2. **Extravasation:** **PACLI**taxel causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.

3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

4. **Drug Interactions:** **PACLI**taxel is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

**Call Dr. Ken Swenerton or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

Date activated: N/A

Date revised: 01 Apr 2011 (estimated GFR capped, reformatted with TALLman lettering)